Case Report

Invasive *Vibrio cholerae* Non-O1 Non-O139 Infection in a Thalassemic Child

Warunee Punpanich MD, PhD*,
Pugpen Sirikutt MD*, Naris Waranawat MD*

**Department of Pediatrics, Queen Sirikit National Institute of Child Health, College of Medicine, Rangsit University, Bangkok, Thailand*

Invasive, extra-intestinal infection with Vibrio cholerae non-O1, non-O139 is rare especially among children. Herein the authors report a 12- year-old girl with underlying β-thalassemia status post-splenectomy presenting with V. cholerae non-O1, non-O139 gastroenteritis with concomitant septicemia. The pathogen was identified from stool and blood culture and the patient recovered uneventfully after antimicrobial and supportive therapy. A review and comparison of clinical manifestations and outcomes with the previous four cases of invasive V. cholerae non-O1, non-O139 in post-splenectomy thalassemic pediatric patients is reported.

Keyword: *Vibrio cholera non-O1, non-O139, Gastroenteritis, Septicemia, Thalassemia, Children*

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Cholera is a contagious disease caused by a pathogenic strain of *V. cholerae*. It can cause massive watery diarrhea with high mortality and morbidity and potential for a large outbreak. *V. cholerae* is a comma-shaped gram-negative bacillus, a member of the family Vibrionaceae. Two major antigenic structures are flagella H and somatic O antigen. Classification into 206 serogroup is based on the O antigen. Only serogroup O1 is a clinically important human pathogen resulting in seven major cholera pandemics between 1,817 and 1,961. The other serogroups are then classified as serogroup non-O1 which is generally a cause of sporadic cases except for serogroup O139 which was responsible for a major outbreak in Bengal, India in 1992[1]. In addition, there has been a local outbreak caused by serogroup O10 and O12 in Peru in 1994[2] and serogroup non-O1 among Khmers in a refugee camp in Aranyaprathet, Thailand in 1990[3]. Transmission occurs mainly through the fecal-oral route or through the consumption of uncooked seafood, or contaminated water. It can also enter the human body through wounds after contact with contaminated water.

Clinical manifestations of *V. cholerae* non-O1 can be classified into 3 patterns as follows. First, there is acute gastroenteritis with typical rice water diarrhea. Some cases may have mucus bloody stool, nausea and vomiting. Symptoms range from mild until severe diarrhea similar to classic cholera[1,4]. Lamahachon conducted a 5-year retrospective review of acute gastroenteritis caused by *V. cholerae* at Queen Sirikit National Institute of Child Health, Bangkok, Thailand from 1999 to 2003[5]. There was total of 262 of *V. cholera* gastroenteritis. Twenty-seven percent (66) of cases were caused by *V. cholerae* O1 or O139 and 73% (196 cases) were caused by *V. cholerae* non-O1, non-O139. The peak season was during summer time especially during the month of May. Clinical manifestations of *V. cholerae* non-O1, non-O139 gastroenteritis included 41% mucous bloody diarrhea, 33% watery diarrhea, 12% soft or liquid (but not watery) stool, 13% without information regarding stool characteristics. Twenty-nine percent had concurrent nausea and vomiting. Forty-nine percent had axillary temperature higher than 37.5°c. There was no fatality case. Significant complications were dehydration, metabolic acidosis, electrolyte imbalance *e.g.*, hypokalemia and hyponatremia. Those infected with *V. cholerae* O1, O139 had a significantly higher rate of complications compared to those infected with *V. cholerae* non-O1,

Correspondence to:
Punpanich W, Department of Pediatrics, Queen Sirikit National Institute of Child Health, Bangkok 10400, Thailand.
Phone: 0-2354-8345
E-mail: warunee@vandepitte.eu

non-O139. No concurrent septicemia was detected in either group. The second pattern, non-bacteremic/non-intestinal infections, includes cellulitis, necrotizing fasciitis, pneumonia, purulent salpingitis and biliary tract infections[4]. The third, bacteremia, is rare but has a high fatality rate ranging from 33 to 61.5%[4,6,7]. Common clinical manifestations include high grade fever, diarrhea and abdominal pain[8-11]. Serious complications including liver and splenic abscess[12], spontaneous bacterial peritonitis[6], hypotension[4,8,10,11], septic shock[13], cerebritis[14], renal failure[15,16], thrombocytopenia can ensue[6]. In addition, there are case reports of meningitis caused by *V. cholerae* non-O1 in neonates and an infant[17-20]. Major risk factors for invasive infections include: 1) infections caused by a polysaccharide capsule-producing serotype[21] which can protect the bacteria from phagocytosis, 2) underlying disease resulting in impaired host defense mechanism *e.g.*, hepatic cirrhosis[4,6,8,22], hematologic malignancy[22], immune deficiency[23], malnutrition[7], bone marrow transplant[24], Fonconi anemia[10] and nephrotic syndrome[9]. *V. cholerae* non-O1 can also cause invasive infections/bacteremia in individuals without underlying illness[12,15,25,26].

Case Report

A 12-year-old Thai girl presented with one day of fever with chill, crampy abdominal pain in the right lower abdomen and one episode of loose stool after ingesting bamboo shoot a day earlier. She appeared to be markedly fatigued and pale. Significant past medical history was β-thalassemia (hemoglobin EF) diagnosed during the first year of life and requiring frequent transfusion every 2-3 months until a splenectomy was performed at the age of 8. Pneumococcal polysaccharide vaccine was given 4 months prior to this admission. Physical examination revealed an ill-appearing young adolescent whose axillary temperature was 39.4°C; heart rate 154 beats/minute; blood pressure 110/70 respiratory rate, 44 breaths/min; and weight, 26.7 Kg). She looked noticeably pale and icteric. Her lungs were clear and her cardiac sounds were normal. Her abdomen was not distended and an apparent old surgical scar from a previous splenectomy could be seen. Liver was slightly enlarged (3 cm below right costal margin). Her hemoglobin level was 5 g/dL and white blood cell count was 31,517 cell/cu.mL with 82% neutrophils, 9% lymphocytes and 8% monocytes and 1% eosinophils. Platelet count was 349,000 cell/mm^3. Other laboratory tests revealed: sodium, 129 mol/L; potassium, 3.9 mmol/L; chloride, 97 mmol/L bicarbonate, 15.9 mmol/L; urea nitrogen, 26 mg/dL; and creatinine, 0.5 mg/dL. A urinalysis revealed: 1.015 specific gravity; 1+ for albumin, urobilinogen, and bilirubin; 3+ blood; 5-10 red blood cell/high power field (HPF); and 2-3 white blood cell/HPF. A liver function test showed increased total bilirubin (14.43 mg/dL), direct bilirubin (1.74 mg/dL), indirect bilirubin (12.69 mg/dL); AST 58 IU/L, ALT 29 IU/L and alkaline phosphatase 185 IU/L. She was diagnosed with acute gastroenteritis with moderate dehydration and acute hemolytic anemia with underlying thalassemia, after which intravenous fluid, packed red cell transfusion, and cefotaxime were administered.

During the first few days of admission the patient remained febrile with persistent abdominal pain and vomiting. Surgical consultation was made due to suspicion of gut obstruction. The patient was put on nothing per oral with retained nasogastric tube and antibiotic treatment. Her abdominal ultrasound revealed unremarkable results except for gallstones without acute cholecystitis. On the second day of admission the patient had frequent, watery diarrhea; however, her temperature began to decline. An initial hemoculture result returned on the next day grew *Vibrio cholerae* non-O1 (non-O139) susceptible to amikacin, ampicillin, cefoperazone/sulbactam, cefotaxime, ceftazidime, ceftriaxone, co-trimoxazole, gentamicin and imipenem. Stool culture grew *Plesiomonas shigelloides* and *V. cholerae* non-O1 (non-O139). *P. shigelloides* was sensitive to co-trimoxazole, gentamicin, norfloxacin and resistant to tetracycline. *V. cholerae* non-O1 (non-O139) was sensitive to co-trimoxazole, and tetracycline. Therefore, the final diagnoses were *V. cholerae* non-O1, non-O139 septicemia, *V. cholerae* non-O1, non-0139 with *P. shigelloides* gastroenteritis with underlying β-thalassemia status post-splenectomy, and acute hemolytic anemia. Fever disappeared on day 2 after antibiotic initiation. Diarrhea and abdominal pain gradually improved and the patients returned to health by day 7 of admission with no significant medical complication. A second hemoculture repeated 24 hours after the initiation of antimicrobial treatment yielded negative result and cefotaxime was continued for 2 weeks.

Discussion

Invasive *V. cholerae* non-O1 infections in thalassemic patients are rare. Existing reports published in the English language are mainly pediatric cases from

Table 1. Clinical characteristics and outcomes of thalassemic patients with invasive *V.cholera* non-O1 infection

	Case1 (1990)[29]	Case 2 (1995)[28]	Case 3 (1996)[27]	Case 4 (1996)[27]	Current case
Age (year)	15	14	17	10	12
Gender	female	female	male	male	female
Type of thalassemia	β-thal HbE	β-thal HbE	Hemozygous β-thalassemia	Hemozygous β-thalassemia	Hemozygous β-thalassemia
Duration after splenectomy (years)	3	2 months	3	5	4
Fever	+	+	+	+	+
Loose stool	+	+	+	+	+
Nausea/vomiting	+	+	-	+	+
Abdominal pain	+	N/A	-	+	+
Shock	+	+	+	-	-
Peritonitis	+	N/A	N/A	+	-
Hemoculture	Positive	Negative	Positive	Positive	Positive

N/A: data not available

Thailand[27-29] and one adult case from Malaysia[30]. Clinical characteristics and outcome of existing pediatric cases are shown in Table 1[27-29]. All cases had positive hemoculture of *V. cholerae* non-O1, except for case number 2 who presented with rapid progressive sepsis, respiratory failure and death within 13 hours after hospitalization. Autopsy revealed massive neutrophil infiltration with hemorrhagic foci in all layers of intestinal mucosa compatible with invasive enterocolitis.

All of these patients had undergone splenectomy prior to invasive *V. cholerae* non-O1 infection. The authors are unable to identify any cases of invasive *V. cholerae* non-O1 infection among thalassemic patients without previous splenectomy. Therefore, it is likely that asplenia is a major risk factor of invasive *V. cholerae* non-O1 infection. Existing literature indicated that those who underwent splenectomy were at a 600 times higher risk of fatal sepsis compared to those who had not had their spleen removed[31].

In conclusion, we reported a rare case of *V. cholerae* non-O1 septicemia in a 14-year-old thalassemic patient status post-splenectomy, with no apparent history of raw seafood consumption prior to the illness. A review of existing cases in pediatric population indicated that this condition mainly occurs in compromised host but can also appear in immunocompetent individuals as well. Findings of the present report suggest that thalassemia post splenectomy increases susceptibility to this infection. Careful handling of food and proper treatment of water before consumption are essential in preventing this condition especially among high risk populations.

Potential conflicts of interest

None.

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การติดเชื้อ *Vibrio cholera non-O1 non-O139* ในกระแสโลหิตของผู้ป่วยเด็ก β-thalassemia

วารุณี พรรณพานิช, พักต์เพ็ญ สิริคุตต์, นริศ วารณะวัฒน์

การติดเชื้อนอกลำไส้ของ Vibrio cholerae ในเด็กมีรายงานน้อยมาก ผู้นิพนธ์ได้รายงานผู้ป่วยเด็กหญิงไทย อายุ 12 ปี มีโรคประจำตัว β-thalassemia และเคยได้รับการตัดม้ามมาก่อน ครั้งนี้มาโรงพยาบาลด้วยการติดเชื้อของระบบทางเดินอาหาร และกระแสโลหิต ในเวลาเดียวกัน ผลการเพาะเชื้อในกระแสโลหิตและในอุจจาระ พบเชื้อ Vibrio cholerae non-O1, non-O139 ผู้ป่วยได้รับการรักษาด้วยยาปฏิชีวนะและการรักษาประคับประคอง จนอาการดีขึ้นเป็นปรกติ ผู้นิพนธ์ได้ทำการทบทวนวรรณกรรมและเปรียบเทียบอาการและผลการตรวจทางห้องปฏิบัติการของผู้ป่วยรายนี้กับรายงานผู้ป่วยเด็กที่เคยมีมาในอดีต